WORLD INTELLECTUAL PROPERTY ORGANIZATION



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:

C07D 211/42, 405/06, 401/12, 405/12, 405/14, A61K 31/445

(11) International Publication Number:

WO 97/30031

(43) International Publication Date:

21 August 1997 (21.08.97)

(21) International Application Number:

PCT/EP97/00584

A1

(22) International Filing Date:

7 February 1997 (07.02.97)

(30) Priority Data:

96200379.4

15 February 1996 (15.02.96) EP

(34) Countries for which the regional or international application was filed:

DE et al.

(71) Applicant (for all designated States except US): JANSSEN PHARMACEUTICA N.V. [BE/BE]; Turnhoutseweg 30, B-2340 Beerse (BE).

(72) Inventors: and

(75) Inventors/Applicants (for US only): BOSMANS, Jean-Paul, R., M., A. [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). LOVE, Christopher, J. [GB/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). DECLEYN, Michel, A., J. [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). D'HAEN, Henri, E., F. [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE).

(81) Designated States: AL, AM, AU, BA, BB, BG, BR, CA, CN. CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, LC, LK, LR. LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG. SI, SK, TR, TT, UA, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

With international search report.

(54) Title: ESTERS OF 3-HYDROXY-PIPERIDINEMETHANOL DERIVATIVES

(57) Abstract

The present invention of compounds of formula (1), a stereochemically isomeric form thereof, an N-oxide form thereof or a pharmaceutically acceptable acid addition salt thereof, R^1 is C_{1-6} alkyloxy, C_{2-6} alkenyloxy or C_{2-6} alkynyloxy; R² is hydrogen or C₁₋₆alkyloxy, or when taken together R¹ and R2 may form a bivalent radical of formula wherein in said bivalent radicals one or two hydrogen atoms may be substituted with C1-salkyl; R3 is hydrogen or halo; R4 is hydrogen or C1.

$$L-N \longrightarrow CH_2-O-C \longrightarrow R^1 \longrightarrow R^2 \longrightarrow NH_2 \qquad (I)$$

6alkyl; L is C₃₋₆cycloalkyl, C₅₋₆cycloalkanone, C₂₋₆alkenyl optionally substituted with aryl, or L is a radical of formula -Alk-R⁵. Alk X-R⁶. -Alk-Y-C(-O)-R⁸, or -Alk-Y-C(-O)-NR¹⁰R¹¹ wherein each Alk is C₁₋₁₂alkanediyl; and R⁵ is hydrogen, cyano. C₁₋₆alkylsultonylarume. C3-6cycloalkyl, C5-6cycloalkanone, aryl, di(aryl)methyl or a heterocyclic ringsystem; R6 is hydrogen, C1-6alkyl, hydroxyC1-6alkyl, C4. 6cycloalkyl, aryl or heterocyclic ringsystem; X is O, S, SO2 or NR?; said R7 being hydrogen, C1-6alkyl or aryl; R8 is hydrogen, C1-6alkyl, C3-6cycloalkyl, aryl, arylC1-6alkyl, di(aryl)methyl, C1-6alkyloxy or hydroxy; Y is NR9 or a direct bond; said R9 being hydrogen, C1-6alkyl or aryl; R10 and R11 each independently are hydrogen, CL salkyl, C3-scycloalkyl, aryl or arylC1 salkyl, or R10 and R11 combined with the nitrogen atom bearing R10 and R11 may form a pyrrolidinyl or piperidinyl ring both being optionally substituted with C1-balkyl, animo or mono or di(C1-6alkyl)amino, or said R¹⁰ and R¹¹ combined with the nitrogen bearing R¹⁰ and R¹¹ may form a piperaziny! Of 4 morphomost radical both being optionally substituted with C1-calkyl. Processes for preparing said products, formulations comprising said products, their use as a medicine are disclosed, in particular for treating conditions which are related to impairment of gastne employing